Clinical and Genetic Analysis of Five Patients with Vitamin D-Dependent Rickets Type 1A

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Introduction

- The CYP27B1 gene encodes 25-hydroxyvitamin D-1α-hydroxylase.
- Mutations of this gene cause vitamin D-dependent rickets type 1A (VDDR-IA, OMIM 264700), which is a rare autosomal recessive disorder.
- Here in we report 5 patients with 1α-hydroxylase deficiencies.

Method

- We studied 5 patients from 3 families who diagnosed as 1α-hydroxylase deficiency genetically.

Results

- All patients had hypocalcemia, hypophosphatemia, hyperphosphatasemia, elevated serum PTH, normal or high vitamin D levels, and low or inappropriately normal calcitriol levels at presentation (Table).
- Patients were diagnosed less than 18 months years old. All patients had a family history of consanguinity.
- Homozygous mutations in the CYP27B1 gene were found in all the patients.
- Four of them have splice donor site mutation in intron 1 (c.195 + 2 T>G), causing partial retention of the intron and a shift in the reading frame.

<table>
<thead>
<tr>
<th></th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>PTH (pg/ml)</th>
<th>25-OHD (ng/ml)</th>
<th>1-25-OHD (pg/ml) N: 25-153</th>
<th>Mutation analyses for CYP27B1 gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>8.0</td>
<td>2.3</td>
<td>441</td>
<td>26</td>
<td>15</td>
<td>Homozygous mutation on intron 1 (c.195 + 2 T&gt;G)</td>
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<tr>
<td>Patient 2</td>
<td>5.9</td>
<td>3.41</td>
<td>925</td>
<td>41</td>
<td>&lt;1.3</td>
<td>Homozygous mutation on egzon 8 p.Phe443Profs*24</td>
</tr>
<tr>
<td>Patient 3</td>
<td>6.2</td>
<td>2.8</td>
<td>980</td>
<td>120</td>
<td>12</td>
<td>Homozygous mutation on intron 1 (c.195 + 2 T&gt;G)</td>
</tr>
<tr>
<td>Patient 4</td>
<td>7.8</td>
<td>3.0</td>
<td>625</td>
<td>45</td>
<td>6</td>
<td>Homozygous mutation on intron 1 (c.195 + 2 T&gt;G)</td>
</tr>
<tr>
<td>Patient 5</td>
<td>8.0</td>
<td>2.9</td>
<td>546</td>
<td>50</td>
<td>11</td>
<td>Homozygous mutation on intron 1 (c.195 + 2 T&gt;G)</td>
</tr>
</tbody>
</table>

Conclusion

- Clinically, all the patients required calcium and calcitriol initially and then continuously calcitriol treatment.
- Autosomal recessive diseases are common in countries where the consanguineous marriages are common.
- VDDR-IA should be kept in mind patients with vitamin D resistant rickets.